

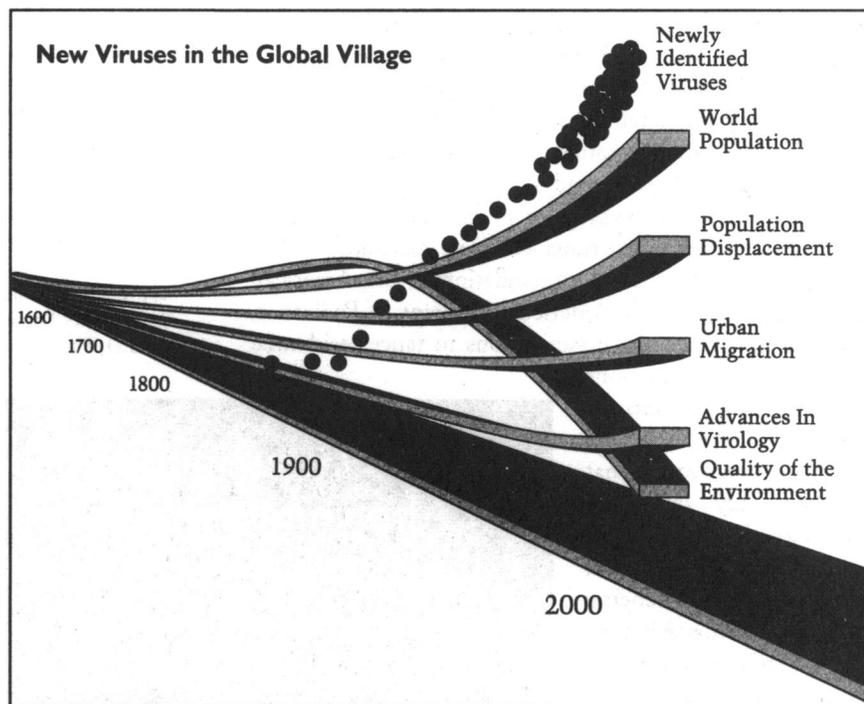
Stalking the Next Epidemic: ProMED Tracks Emerging Diseases

JACK WOODALL, PHD

Ask anyone today what infectious disease they fear the most, and chances are the reply will be not "AIDS" but "Ebola." The publicity given to the recent outbreaks of this disease has made the serpent-shaped virus the poster child for emerging diseases. But HIV and Ebola virus are not alone. We also have to fear hantaviruses, new strains of plague, and a whole host of other emerging or reemerging infections.

Bioterrorism is another perceived threat that has been in the news in recent months. The continuing revelations of Iraq's extensive biowarfare program add to the concern. There have even been suggestions from some quarters in recent years that the dengue hemorrhagic fever epidemics in Cuba and Nicaragua and the 1994 plague outbreak in India were due to biological attacks.

Would the 1995 outbreak of Ebola have come to the attention of the Zairian health authorities—let alone the world—if an Italian nun working at the hospital had not died of it? (Unfortunately, news services pick up the occasional unexplained death of an expatriate rather than the hundreds of similar deaths of local people.) And once word gets out of an outbreak, is there the local expertise to diagnose the cause so that specific countermeasures can be taken? It took months for the first recorded epidemic of yellow fever in Kenya, which occurred in



While the world population soars and the quality of the environment plummets, the number of newly identified viruses explodes. These viruses are the causes of emerging diseases in humans, animals, and plants that may have a devastating impact on the world's health.

SOURCE: Mann J, Tarantola DJM, Netter TW. AIDS in the world. Cambridge (MA): Harvard University Press, 1992:827.

1992–1993, to be diagnosed locally. In contrast, the 1994 plague outbreak in India was hastily overdiagnosed, which resulted in needless panic in several neighboring and other countries. What is needed is a global network of reliable disease monitoring centers and a rapid communications system connecting them with health institutions around the world. Newly available technology now puts these lofty ideals within reach.

It has been claimed that if we had only recognized HIV when it first appeared, we would have had several years' start on containing it and on the research we are now doing to identify preventive measures and treatment. If the world community is ever going to be able to nip emerging diseases in the bud, we have to be able to recognize the bud. The same applies to the use

of biological agents such as anthrax in war or terrorist attacks or to accidents occurring during the production or transport of a biological weapons agent. The emerging infectious diseases and potential biological weapons agents we should be concerned about today include a new, more virulent, strain of influenza; anthrax; botulinum toxin; cholera; plague; yellow fever and other hemorrhagic fevers; Venezuelan equine encephalitis; bat rabies viruses; karnal bunt disease of wheat; and fungal diseases of potatoes. This list includes for good reason some agents that infect animals and plants; they affect our food security, and large scale outbreaks in livestock or crop plants—whether of natural or artificial origin—could produce economic destabilization in the victimized country. Remember the story of the Irish

potato famine 150 years ago?

The U.S. Centers for Disease Control and Prevention's (CDC) world-renowned Epidemic Intelligence Service has gained an enviable reputation for rapid response to reports of epidemics and thorough investigation of every imaginable type of disease or health problem all over the world. The key words here are "response to reports" and "thorough investigation." Before there can be a response, there must be a report. Once there is a report, there should be an investigation.

In January 1996, Joshua Lederberg wrote that concerning world health, "we have never been more vulnerable...."¹ The first need is for "concerted global and domestic surveillance and diagnosis of disease outbreaks and endemic occurrence. This must entail the installation of sophisticated laboratory capabilities at many centers now lacking them."¹ But in spite of the urgency of the situation, "tangible responses by government in the form of budgetary or staffing commitments remain negligible."¹

Communications

There is one thing that is vital to the functioning of a global network of monitoring centers: rapid communications. It is essential that centers be able to instantly communicate laboratory results and situation updates on outbreak investigations to national and international authorities. Telephone and fax are of course standard equipment, but in this day and age nothing beats full Internet access. Detailed laboratory results, X-rays, EKGs, EEGs, three-dimensional CT scans, and even the sounds of a patient's heartbeat; digital color videos and photographs of external signs such as rashes and bite marks, of internal organs, of pathology slides, or of the shape and color of an infected plant leaf; or computer-enhanced satellite images of croplands showing infected areas in a contrasting color—all can be transmitted across the world for examination by experts, wherever they may be.

Electronic communications can also be used to vastly expand the base of surveillance for unusual outbreaks. The dream is to link clinical and health research facilities around the globe so that newly emerging diseases can be recognized early and dealt with rapidly. This is now achievable through the Internet. What has been achieved so far are a number of partial networks and one global one: the ProMED project and its communications arm, ProMED-mail.

The Federation of American Scientists ProMED Project

The Federation of American Scientists (FAS), sponsored by over 40 American Nobel prize winners, has been a center of policy research, analysis, and education for over 50 years. FAS originally undertook ProMED, a project to promote the establishment of a global Program to Monitor Emerging Diseases, as a basis for the international technological cooperation in the prevention of disease called for under the Biological Weapons Convention. At the project's founding conference in Geneva in 1993, which was cosponsored by FAS and WHO, ProMED was given a mandate by 60 prominent health experts from all parts of the world to assure the design, promotion, and implementation of a global program in consultation with appropriate international, national, and nongovernmental agencies.

Since then, ProMED has been in the vanguard of efforts to monitor the increasingly globalized threat of infectious diseases, with two major achievements to date: the drafting of a detailed proposal for a demonstration network of monitoring centers² and the establishment of the first and only publicly accessible global source of timely information on outbreaks, ProMED-mail.

At the 1993 conference, ProMED working groups began to elaborate plans for a global monitoring network; these plans were further developed through subsequent meetings and consultations with more than 300

experts around the world under the guidance of a ProMED Steering Committee. The resulting document proposes a research program to demonstrate the feasibility of a network of centers to monitor emerging diseases directly through clinical surveillance for selected syndromes coupled with effective laboratory back-up. With financial resources in short supply, a small network of strategically located sentinel centers, with capability for surveillance of both endemic and emerging diseases, may be the most effective way, in the near term, not only to test the concept but to begin providing early warning of serious epidemics.

The ProMED project has compiled information on medical centers around the world and identified likely candidate centers for the network. Representatives of some of these centers came together in February 1996 to exchange information at an international conference on Enhancing Infectious Disease Monitoring and Response organized by ProMED members at the request of the Rockefeller Foundation.

Overview of the ProMED Proposal: Outline for a Demonstration Program

Given current financial constraints in the health sector, what can be foreseen is a painfully slow evolution of national and regional surveillance systems toward the distant goal of a unified global system for monitoring emerging diseases. For more rapid progress, significant investment will be needed for coordination and for developing diagnostic and surveillance capabilities in health institutions in those environments where diseases are most likely to emerge. ProMED proposes making a modest start on this track by prioritizing a small number of strategically situated Third World institutions, mainly those least in need of upgrading, for development as sentinel centers. In this way a functional, although limited, network could be rapidly established at minimal cost.

The system would serve as an experimental model for future expansion.

The centers would start by monitoring the emergence of a limited number of defined syndromes through broadly based local clinical outreach from each center. Each center would develop laboratory capabilities for identifying the likely agents for the targeted syndromes as well as for well-known globally and locally endemic diseases. In developing countries, locally endemic diseases will generally overshadow emerging diseases and will therefore be the main focus of concern as well as these centers' incentive for undertaking the program. The goal would be to achieve full competence at each center within, at most, five years and then begin to expand the number of syndromes monitored. If successful, the number of centers could be increased, as resources permit, to cover more areas of the world.

The plan calls for the formation of a network consisting of, roughly, 10 of the most adequately prepared medical facilities in different regions of the developing world. Agreement and cooperation of the government would be essential in each case. Each center would develop its own local/regional network including clinics, hospitals, health care providers, academic centers, government agencies, and voluntary organizations with which it would cooperate and exchange information. The centers would collect clinical data and diagnostic samples with the help of these networks. The centers and their networks would be assisted in developing expertise in recognizing and diagnosing the specified syndromes and would have access to designated specialized reference laboratories.

Concentration on a small number of strategically located medical facilities in developing countries to create comprehensive centers of excellence would establish regional nuclei in areas critical for monitoring emerging diseases. The centers would reach out to other institutions in their regions, providing med-

ical information and training.

The process would be coordinated by a program office, which could be located at one of the centers or at a separate location. The program office, in collaboration with various programs at WHO, would maintain the network's level of competence through a quality assurance program and would provide diagnostic materials and equipment where needed as well as training activities and regular meetings of center heads for coordination and exchange of experience. The program office would also solicit, and help to

Through the Internet, we can link clinical and health research facilities around the globe so that newly emerging diseases can be recognized early and dealt with rapidly.

raise, financial support for individual centers to cover other needs. The centers would be linked to the program office with an electronic communications system, through which surveillance information would be reported in a timely manner and relayed to alert other centers and interested institutions. The network would coordinate with existing networks such as WHONET (a global reporting system for antibiotic resistance) and other WHO electronic reporting systems that may be established, with the goal of forming a unified global communi-

cations system on infectious disease surveillance that will incorporate data from existing and future international, regional, national, and local surveillance efforts.

WHO may find it difficult to undertake even a limited trial program such as this in view of its resource limitations. Therefore, a demonstration program could perhaps be established outside WHO as a research project which, if successful, would eventually expand and merge with other surveillance activities at WHO.

Although the initial program must deal primarily with human disease, it could expand later to include veterinary centers and animal diseases, and preliminary feelers are already being put out in that direction. ProMED is developing a separate plan for monitoring emerging plant diseases.

ProMED-mail

Rather than wait until a comprehensive program is funded and implemented by some international agency, the ProMED Steering Committee decided to initiate an e-mail network for rapid reporting and discussion of emerging infectious disease outbreaks. Thus on 19 August 1994 a public e-mail network was born, now known as ProMED-mail. Over the last two years the list has grown to over 7000 direct subscribers from more than 125 countries. Literally thousands of other people receive the information through secondary distribution or visit one of the four sites on the World Wide Web that carry ProMED-mail posts.

The mission of ProMED-mail is fourfold. First and foremost, it is to provide one-stop shopping for early reports of emerging and reemerging infectious disease outbreaks throughout the world. In order to reach the largest possible number of countries, it is based on e-mail because more countries, and more people in many countries, currently have e-mail than have the full Internet access required to reach the Web. ProMED-mail receives WHO's disease bulletins and

the reports of the International Office of Epizootics and the European and Mediterranean Plant Protection Organization over the Internet as they are issued. CDC sends regular updates of the hantavirus pulmonary syndrome (HPS) situation in the United States. The State Epidemiologist for Russia has sent regular information on infectious diseases for posting. The Chief Veterinary Officers of Australia and New Zealand have sent us official information on outbreaks by e-mail, and we will shortly be receiving the monthly reports on vesicular diseases of livestock in the Americas from the Pan-American Foot-and-Mouth Disease Center. We have volunteers searching the media and the Internet looking for reports of outbreaks in humans, animals, and plants that are attributed to infectious disease, including those due to antibiotic-resistant organisms. We also have colleagues who subscribe to other Internet discussion groups such as those on virology, BSE ("mad cow disease"), and mosquitoes and forward relevant information.

We encourage first-person reports of unusual cases since an outbreak always starts with a single case. But we impose two conditions. Reports cannot be anonymous, and all are reviewed by a member of our panel of experts in human, animal, and plant diseases to cull irrelevant or dubious reports. Approximately half of our subscribers appear to be interested students or people who are not in the health or biomedical professions but whose wide geographic distribution gives us global coverage that official disease surveillance systems cannot duplicate.

Second, our mission is to permit rapid exchange of information on all aspects of emerging and reemerging infectious diseases. Well over 100 staff members of CDC subscribe along with officials of health departments in many states of the United States, medical staff with U.S. forces worldwide, the U.S. Department of Agriculture, the Food and Drug Administration, and the National Institutes of

Health of both the United States and Japan as well as experts at Britain's Public Health Laboratory Service, France's Pasteur Institutes around the world, the state epidemiologists of Russia, Sweden, and Zimbabwe, and universities everywhere. This is an enormous pool of expertise capable of answering practically any query that is raised about a case or outbreak of a rare but emerging disease. Subscribing physicians and public health workers in any country receive a rapid response to their urgent questions with recommendations for prevention, treatment,

With financial resources in short supply, a small network of strategically located sentinel centers may be the most effective way to begin providing early warning of serious epidemics.

and control. For example, ProMED-mail has recently elicited responses from subscribers to requests on how to treat conditions as disparate as enterohemorrhagic *E. coli* infection and thallium poisoning.

Third, we strive to increase intraregional communication and information sharing about emerging diseases within the developing world. Many of the emerging diseases that most concern people today, such as Ebola, plague, and dengue hemorrhagic fever, have arisen in the developing world, where communications are neither rapid nor reliable and

where information in the form of paper documentation is scarce. Yet there is a latent, unpublished, and untapped reservoir of information about those diseases and others of potential concern to the industrialized world. An example is the response to a query from South Africa asking if anyone had any experience in using a particular drug to treat a sexually transmitted disease. Back came a reply from Mozambique saying that, indeed, the drug works and giving the dosage. It is this sort of information that is now being exchanged through ProMED-mail and that is filed in archives that are searchable by keyword.

We are also conscious of the need to exchange information in languages other than English. Preliminary contacts are being made to establish regional e-mail networks operating in French, Spanish, and Portuguese.

Fourth, we aim to encourage collaboration among specialists in different fields and in different locations. As mentioned, ProMED-mail reports outbreaks in humans, animals, and plants. We aim to raise consciousness about the fact that our health security is affected by diseases that attack our food animals, crops, and wildlife at least as much as by human diseases. Food shortage leads to malnutrition, leading in turn to a depressed immune system and increased susceptibility to environmental and other microbes that normally do not produce human disease. Developments in techniques for the isolation and identification of viruses and other disease agents in the animal or plant field may have applications in human medicine, and vice versa. The expert's way of looking at epidemic disease in one of those fields could lead to insights that are useful in another field.

It may be questioned what ProMED-mail, which is an unofficial reporting system, can do that is not already being done by international and national disease reporting systems. The fact is that official systems, even WHO's, are not yet fully functional on a global scale, and they are all bound by bureaucratic constraints that require

clearances at various levels before publication, leading to delays in warning other countries about a possible problem. There are even countries that forbid WHO to report to the world that an outbreak is occurring on their territory because they are afraid of repercussions on trade or tourism.

Satellife, HealthNet, and the Outbreak Website

The encumbrances on official reporting and the success of ProMED-mail have demonstrated the value of an independent, nongovernmental rapid reporting system. Therefore, although ProMED-mail was originally conceived as a model and stop-gap measure, it has now been put on a permanent basis, with professional rather than volunteer management. In August 1996, FAS turned over the management and financing of ProMED-mail to SatelliLife, a non-profit medical communications organization. FAS continues to host the ProMED-mail Policy Committee, under the chairmanship of the author.

SatelliLife is the communications arm of International Physicians for the Prevention of Nuclear War (IPPNW), which has received the Nobel Prize for its work. Several years ago, IPPNW began a unique experiment by launching a low-level satellite into polar orbit—which means that it covers every point on earth, as the Earth rotates below it, two or three times a day, with a transmission window of a few minutes on each pass. SatelliLife then installed ultra-low-cost ground stations, consisting of little more than a computer, a sideband radio, and a satellite dish, in key medical schools in developing countries. At each pass of the satellite over the ground station, the medical librarian can upload literature search requests and e-mail messages and download the replies from the previous pass. These are delivered over telephone lines or ground radio links to and from the computers of

local subscribers through what is known as HealthNet. HealthNet traffic includes a digest of selected articles from current medical journals, ProMED-mail posts, and posts from similar programs sponsored by SatelliLife called ProCAARE, the Program for Collaboration Against AIDS and Related Epidemics, and e-drug, which deals with essential drugs.

The OUTBREAK Website is the brainchild of David Ornstein, a software developer in California. Originally called the Ebola Page, it was designed at the time of the Ebola outbreak in Kikwit, Zaire, to provide links to all the information on the Web about that disease. It became wildly popular—it received one quarter of a million hits during the epidemic—and won several Internet awards. When the Kikwit outbreak died out, many people both within and outside the public health arena urged him to expand the site to provide the answers to frequently asked questions about other emerging diseases. The site, still winning awards, now provides extensive information on a range of diseases for anyone with Web access, including links to the ProMED-mail archives on the relevant diseases. A merger of ProMED-mail and OUTBREAK is under discussion.

Conclusion

Millions of people criss-cross the globe daily by air, and many of them pass through gateway airports in the United States. The speed of air travel means that inevitably some of them become infected in another country and leave it while still healthy only to fall ill and transmit the disease to others on arrival in the United States or while in transit through a gateway. During the 1994 plague outbreak in India, more than 2000 passengers a day arrived at New York City airports from India. Ten of them showed suspicious symptoms on arrival and were quarantined. Fortunately, none of them was a carrier. One traveler fell ill in Chicago with Lassa fever, a hemorrhagic disease, after arriving from

Africa some years back; another died of yellow fever in Tennessee in August 1996 after returning from a fishing trip on the Amazon. Dozens of people return to the United States every year infected with dengue fever. Early reporting of, and response to, outbreaks of such diseases at their source will alert physicians in this country and help them treat affected patients and counsel potential travelers about the need for protective vaccinations. The ProMED initiative responds to this need.

It is generally agreed that to safeguard the security of human health, a global surveillance system capable of rapid reporting and investigation of new disease outbreaks is essential. This is true regardless of whether an outbreak is of natural origin or is of artificial origin—as in biowarfare or a bioterrorist attack. The ProMED proposal for a Demonstration Program for Monitoring Emerging Diseases and ProMED-mail, the global public e-mail network for reporting outbreaks, are steps toward implementing such a system.

Dr. Woodall is the Director of FAS ProMED-mail and the Director of the Arbovirus Laboratory, Wadsworth Center, New York State Department of Health.

To subscribe to ProMED-mail, send to <majordomo@usa.healthnet.org> the text: subscribe promed. The Website addresses are: www.healthnet.org/programs/promed.html and www.outbreak.org/.

Address correspondence to Dr. Woodall, Griffin Laboratory, 5668 State Farm Road, Slingerlands NY 12159; tel. 518-869-4524; fax 518-869-4530; e-mail <woodall@wadsworth.org>.

References

1. Lederberg J. Infection emergent. JAMA 1996;275:243-245.
2. Morse SS. Global monitoring of emerging diseases: design for a demonstration program. Health Policy. In press.